

DOCKET NO.: JANS-0027/JAB1498 US  
 Application No.: 10/030,202  
 Office Action Dated: October 20, 2004

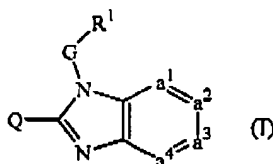
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This listing of claims will replace all prior versions, and listings, of claims in the application.

***Listing of Claims:***

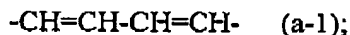
1. *(previously presented)* A method for treating respiratory syncytial viral infections, comprising the step of:

administering to a patient in need of such treatment, a composition comprising an effective amount of a compound of formula I:

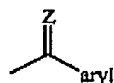


an addition salt or stereochemically isomeric form thereof,

wherein  $-a^1=a^2-a^3=a^4-$  represents a bivalent radical of formula

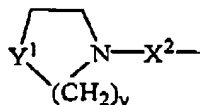
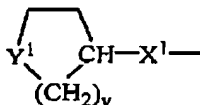
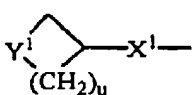


wherein each hydrogen atom in the radical (a-1) may optionally be replaced by halo, C<sub>1-6</sub>alkyl, nitro, amino, hydroxy, C<sub>1-6</sub>alkyloxy, polyhaloC<sub>1-6</sub>alkyl, carboxyl, aminoC<sub>1-6</sub>alkyl, mono- or di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, hydroxyC<sub>1-6</sub>alkyl, or a radical of formula



wherein Z is O, CH-C(=O)-NR<sup>5a</sup>R<sup>5b</sup>, CH<sub>2</sub>, CH-C<sub>1-6</sub>alkyl, N-OH or N-O-C<sub>1-6</sub>alkyl;

Q is a radical of formula



(b-4)

(b-5)

or,

(b-6)

;

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wherein

 $Y^1$  is a bivalent radical of formula  $-NR^2-$  or  $-CH(NR^2R^4)-$ ; $X^1$  is  $NR^4$ , S,  $S(=O)$ ,  $S(=O)_2$ , O,  $CH_2$ ,  $C(=O)$ ,  $C(=CH_2)$ ,  $CH(OH)$ ,  $CH(CH_3)$ ,  $CH(OCH_3)$ ,  $CH(SCH_3)$ ,  $CH(NR^{5a}R^{5b})$ ,  $CH_2-NR^4$  or  $NR^4-CH_2$ ; $X^2$  is a direct bond,  $CH_2$ ,  $C(=O)$ ,  $NR^4$ ,  $C_{1-4}alkyl-NR^4$ ,  $NR^4-C_{1-4}alkyl$ ;

u is 2 or 3;

v is 2; and

whereby each hydrogen atom in the carbocycles and the heterocycles defined in radicals (b-4), (b-5), and (b-6) may optionally be replaced by  $R^3$ ; with the proviso that when  $R^3$  is hydroxy or  $C_{1-6}alkyloxy$ , then  $R^3$  can not replace a hydrogen atom in the  $\alpha$  position relative to a nitrogen atom;

G is a direct bond or  $C_{1-10}alkanediyl$ ;

$R^1$  is a monocyclic heterocycle selected from piperidiny, piperaziny, pyridyl, pyraziny, pyridaziny, pyrimidiny, pyrroly, furanyl, tetrahydrofuranyl, thienyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, and isothiazolyl; and each heterocycle may optionally be substituted with 1 or where possible more substituents selected from halo, hydroxy, amino, cyano, carboxy,  $C_{1-6}alkyl$ ,  $C_{1-6}alkyloxy$ ,  $C_{1-6}alkylthio$ ,  $C_{1-6}alkyloxyC_{1-6}alkyl$ , aryl,  $arylC_{1-6}alkyl$ ,  $arylC_{1-6}alkyloxy$ ,  $hydroxyC_{1-6}alkyl$ , mono-or di( $C_{1-6}alkyl$ )amino, mono-or di( $C_{1-6}alkyl$ )amino $C_{1-6}alkyl$ , polyhalo $C_{1-6}alkyl$ ,  $C_{1-6}alkylcarbonylamino$ ,  $C_{1-6}alkyl-SO_2-NR^{5c}$ ,  $aryl-SO_2-NR^{5c}$ ,  $C_{1-6}alkyloxycarbonyl$ ,  $-C(=O)-NR^{5c}R^{5d}$ ,  $HO(-CH_2-CH_2-O)_n$ ,  $halo(-CH_2-CH_2-O)_n$ ,  $C_{1-6}alkyloxy(-CH_2-CH_2-O)_n$ ,  $arylC_{1-6}alkyloxy(-CH_2-CH_2-O)_n$  and mono-or di( $C_{1-6}alkyl$ )amino $(-CH_2-CH_2-O)_n$ ;

each n independently is 1, 2, 3 or 4;

$R^2$  is hydrogen, formyl,  $C_{1-6}alkylcarbonyl$ , Hetercarbonyl, pyrrolidiny, piperidiny, homopiperidiny,  $C_{3-7}cycloalkyl$  substituted with  $N(R^6)_2$ , or  $C_{1-10}alkyl$  substituted with  $N(R^6)_2$  and optionally with a second, third or fourth substituent selected from amino, hydroxy,  $C_{3-7}cycloalkyl$ ,  $C_{2-5}alkanediyl$ , piperidiny, mono-or

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di(C<sub>1-6</sub>alkyl)amino,

C<sub>1-6</sub>alkyloxycarbonylamino, aryl and aryloxy;

R<sup>3</sup> is hydrogen, hydroxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, arylC<sub>1-6</sub>alkyl or arylC<sub>1-6</sub>alkyloxy;

R<sup>4</sup> is hydrogen, C<sub>1-6</sub>alkyl or arylC<sub>1-6</sub>alkyl;

R<sup>5a</sup>, R<sup>5b</sup>, R<sup>5c</sup> and R<sup>5d</sup> each independently are hydrogen or C<sub>1-6</sub>alkyl; or

R<sup>5a</sup> and R<sup>5b</sup>, or R<sup>5c</sup> and R<sup>5d</sup> taken together form a bivalent radical of formula -(CH<sub>2</sub>)<sub>s</sub>- wherein s is 4 or 5;

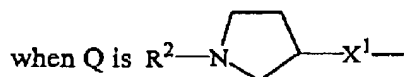
R<sup>6</sup> is hydrogen, C<sub>1-6</sub>alkyl, formyl, hydroxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl or C<sub>1-6</sub>alkyloxycarbonyl;

aryl is phenyl or phenyl substituted with 1 or more-substituents selected from halo, hydroxy, C<sub>1-6</sub>alkyl, hydroxyC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkyloxy; and

Het is pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl;

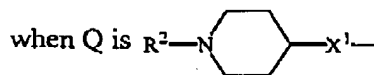
2. (cancelled)

3. (previously presented) A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



wherein X<sup>1</sup> is NR<sup>4</sup>, O, S, S(=O), S(=O)<sub>2</sub>, CH<sub>2</sub>, C(=O), C(=CH<sub>2</sub>) or CH(CH<sub>3</sub>), then R<sup>1</sup> is other than pyridyl, pyridyl substituted with C<sub>1-6</sub>alkyl, pyrimidinyl, pyrazinyl, imidazolyl and imidazolyl substituted with C<sub>1-6</sub>alkyl.

4. (previously presented) A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



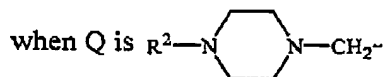
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wherein  $X^1$  is  $NR^4$ , O, S,  $S(=O)$ ,  $S(=O)_2$ ,  $CH_2$ ,  $C(=O)$ ,  $C(=CH_2)$  or  $CH(CH_3)$ , then  $R^1$  is other than pyridyl, pyridyl substituted with  $C_{1-6}$ alkyl, pyridyl substituted with 1 or 2  $C_{1-6}$ alkyloxy, pyrazinyl, pyrrolyl, pyrrolyl substituted with  $C_{1-6}$ alkyl, imidazolyl and imidazolyl substituted with  $C_{1-6}$ alkyl.

5. (cancelled)

6. (previously amended) A method of treating a respiratory syncytial viral infection according to claim 10, wherein:



then  $R^1$  is other than pyridyl, pyrimidinyl, pyrazinyl, imidazolyl and imidazolyl substituted with  $C_{1-6}$ alkyl.

7. (cancelled)

8. (currently amended) A method of treating a respiratory syncytial viral infection comprising the step of administering a therapeutically effective amount of a compound, according to claim 10, wherein the compound is:

(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidinyl]amino]-7-methyl-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol tetrahydrochloride monohydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-1H-benzimidazol-1-yl]methyl]-3-pyridinol;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-6-chloro-1-[(1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine monohydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-6-chloro-1-[(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine;

N-[1-(2-aminoethyl)-4-piperidinyl]-1-[[3-(2-ethoxyethoxy)-6-methyl-2-pyridinyl]methyl]-1H-benzimidazol-2-amine tetrahydrochloride dihydrate;

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(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-chloro-1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-6-chloro-1-[(2-chloro-1,4-dimethyl-1H-imidazol-5-yl)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-6-methyl-1-[(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine;

(±)-N-[1-(2-aminopropyl)-4-piperidinyl]-1-[(3,5,6-trimethylpyrazinyl)methyl]-1H-benzimidazol-2-amine tetrahydrochloride trihydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(3,5,6-trimethylpyrazinyl)methyl]-1H-benzimidazol-2-amine;

N-[1-(2-aminoethyl)-4-piperidinyl]-1-[[3-(2-chloroethoxy)-6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine trihydrochloride dihydrate;

(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(3-amino-2-pyridinyl)methyl]-1H-benzimidazol-2-amine tetrahydrochloride trihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-6-chloro-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride 2-propanolate (1:1);

(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidinyl]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol;

(±)-2-[[2-[[1-(2-aminopropyl)-4-piperidinyl]amino]-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride trihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-7-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride dihydrate;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-6-bromo-4-methyl-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride;

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-1H-benzimidazol-1-yl)methyl]-6-methyl-3-pyridinol tetrahydrochloride monohydrate;

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(±)-2-[[2-[[1-(2-amino-3-methylbutyl)-4-piperidinyl]amino]-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol;  
(±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-[(6-methyl-2-pyridinyl)methyl]-1H-benzimidazol-2-amine; or  
an addition salt or stereochemically isomeric form thereof.

9. *(currently amended)* A method of treating a respiratory syncytial viral infection comprising the step of administering a therapeutically effective amount of a compound, according to claim 10, wherein the compound is:

2-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-5-chloro-7-methyl-1H-benzimidazol-1-yl]methyl]-6-methyl-3-pyridinol tetrahydrochloride tetrahydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2,4-dimethyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2,5-dimethyl-4-oxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(5-methyl-3-isoxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine monohydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-(4-thiazolylmethyl)-1H-benzimidazol-2-amine;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]-1H-benzimidazol-2-amine trihydrochloride;  
5-[[2-[[1-(2-aminoethyl)-4-piperidinyl]amino]-1H-benzimidazol-1-yl]methyl]-2-oxazolemethanol tetrahydrochloride dihydrate;  
N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(3-methyl-5-isoxazolyl)methyl]-1H-benzimidazol-2-amine trihydrochloride monohydrate;

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4-[[1-[[2-(dimethylamino)-4-thiazolyl]methyl]-1H-benzimidazol-2-yl]methyl]-1-piperidineethanamine tetrahydrochloride monohydrate 2-propanolate (1:1);

ethyl 5-[[2-[[1-[2-[[1,1-dimethylethoxy)carbonyl]amino]ethyl]-4-piperidinyl]amino]-1H-benzimidazol-1-yl]methyl]-2-methyl-4-oxazolecarboxylate;

4-[[1-[(2-methyl-4-thiazolyl)methyl]-1H-benzimidazol-2-yl]methyl]-1-piperidineethanamine;

N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-methyl-3-furanyl)methyl]-1H-benzimidazol-2-amine;

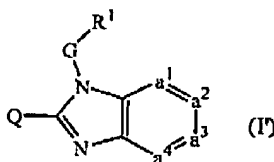
1,1-dimethylethyl 4-[[1-[[3-[2-(dimethylamino)ethoxy]]-6-methyl-2-pyridinyl]methyl]-1H-benzimidazol-2-yl]amino]-1-piperidinecarboxylate;

ethyl 4-[[1-[(3-amino-2-pyridinyl)methyl]-1H-benzimidazol-2-yl]amino]-1-piperidinecarboxylate;

N-[1-(6-methyl-2-pyridinyl)-1H-benzimidazol-2-yl]-1-(3-pyridinylcarbonyl)-4-piperidinamine; or

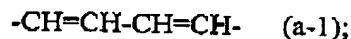
an addition salt or stereochemically isomeric form thereof.

10. *(previously presented)* A method of treating a respiratory syncytial viral infection, comprising the step of administering a therapeutically effective amount of said compound of formula (I'):



an addition salt, or stereochemically isomeric form thereof,

wherein  $-a^1=a^2-a^3=a^4-$  represents a radical of formula



wherein each hydrogen atom in the radicals (a-1) may optionally be replaced by halo,  $\text{C}_{1-6}$ alkyl, nitro, amino, hydroxy,  $\text{C}_{1-6}$ alkyloxy, polyhalo $\text{C}_{1-6}$ alkyl, carboxyl,

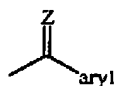
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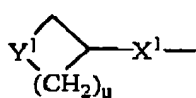
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aminoC<sub>1-6</sub>alkyl, mono- or di(C<sub>1-4</sub>alkyl)aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, hydroxyC<sub>1-6</sub>alkyl, or a radical of formula

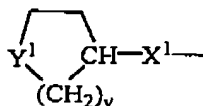


wherein Z is O, CH-C(=O)-NR<sup>5a</sup>R<sup>5b</sup>, CH<sub>2</sub>, CH-C<sub>1-6</sub>alkyl, N-OH or N-O-C<sub>1-6</sub>alkyl;

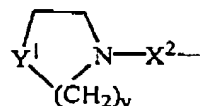
Q is a radical of formula



(b-4)



(b-5)



(b-6)

;

wherein

Y<sup>1</sup> is a bivalent radical of formula -NR<sup>2</sup>- or -CH(NR<sup>2</sup>R<sup>4</sup>)-;

X<sup>1</sup> is NR<sup>4</sup>, S, S(=O), S(=O)<sub>2</sub>, O, CH<sub>2</sub>, C(=O), C(=CH<sub>2</sub>), CH(OH), CH(CH<sub>3</sub>), CH(OCH<sub>3</sub>), CH(SCH<sub>3</sub>), CH(NR<sup>5a</sup>R<sup>5b</sup>), CH<sub>2</sub>-NR<sup>4</sup> or NR<sup>4</sup>-CH<sub>2</sub>;

X<sup>2</sup> is a direct bond, CH<sub>2</sub>, C(=O), NR<sup>4</sup>, C<sub>1-4</sub>alkyl-NR<sup>4</sup>, NR<sup>4</sup>-C<sub>1-4</sub>alkyl;

u is 2 or 3;

v is 2; and

whereby each hydrogen atom in the carbocycles and the heterocycles defined in radicals (b-4), (b-5), and (b-6) may optionally be replaced by R<sup>3</sup>; with the proviso that when R<sup>3</sup> is hydroxy or C<sub>1-6</sub>alkyloxy, then R<sup>3</sup> can not replace a hydrogen atom in the α position relative to a nitrogen atom;

G is a direct bond or C<sub>1-10</sub>alkanediyl;

R<sup>1</sup> is a monocyclic heterocycle selected from pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, pyrrolyl, imidazolyl and pyrazolyl; and each heterocycle may optionally be substituted with 1 or where possible more substituents selected from halo, hydroxy, amino, cyano, carboxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkylthio, C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkyl, aryl, arylC<sub>1-6</sub>alkyl, arylC<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyl, mono- or di(C<sub>1-6</sub>alkyl)amino, mono- or di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, polyhaloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonylamino,



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$C_{1-6}$ alkyl-SO<sub>2</sub>-NR<sup>5c</sup>-, aryl-SO<sub>2</sub>-NR<sup>5c</sup>-,  $C_{1-6}$ alkyloxycarbonyl, -C(=O)-NR<sup>5c</sup>R<sup>5d</sup>,  
 HO(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-, halo(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-,  $C_{1-6}$ alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-,  
 aryl $C_{1-6}$ alkyloxy(-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>- and mono-or di( $C_{1-6}$ alkyl)amino  
 (-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-;

each n independently is 1, 2, 3 or 4;

R<sup>2</sup> is hydrogen, formyl, pyrrolidinyl, piperidinyl, homopiperidinyl,  
 $C_{3-7}$ cycloalkyl substituted with N(R<sup>6</sup>)<sub>2</sub>, or  $C_{1-10}$ alkyl substituted with N(R<sup>6</sup>)<sub>2</sub> and  
 optionally with a second, third or fourth substituent selected from amino, hydroxy,  $C_{3-7}$   
 cycloalkyl,  $C_{2-5}$ alkanediyl, piperidinyl, mono-or di( $C_{1-6}$ alkyl)amino,  
 $C_{1-6}$ alkyloxycarbonylamino, aryl and aryloxy;

R<sup>3</sup> is hydrogen, hydroxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy, aryl $C_{1-6}$ alkyl or  
 aryl $C_{1-6}$ alkyloxy;

R<sup>4</sup> is hydrogen,  $C_{1-6}$ alkyl or aryl $C_{1-6}$ alkyl;

R<sup>5a</sup>, R<sup>5b</sup>, R<sup>5c</sup> and R<sup>5d</sup> each independently are hydrogen or  $C_{1-6}$ alkyl; or

R<sup>5a</sup> and R<sup>5b</sup>, or R<sup>5c</sup> and R<sup>5d</sup> taken together form a bivalent radical of formula -  
 (CH<sub>2</sub>)<sub>s</sub>- wherein s is 4 or 5;

R<sup>6</sup> is hydrogen,  $C_{1-4}$ alkyl, formyl, hydroxy $C_{1-6}$ alkyl,  $C_{1-6}$ alkylcarbonyl or  
 $C_{1-6}$ alkyloxycarbonyl;

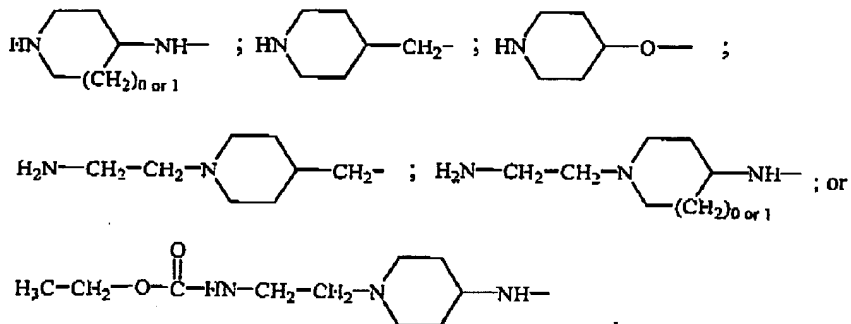
aryl is phenyl or phenyl substituted with 1 or more substituents selected from  
 halo, hydroxy,  $C_{1-6}$ alkyl, hydroxy $C_{1-6}$ alkyl, polyhalo $C_{1-6}$ alkyl, and  $C_{1-6}$ alkyloxy;

provided:

that when G is methylene, and R<sup>1</sup> is 2-pyridyl, 3-pyridyl, 6-methyl-2-  
 pyridyl, 2-pyrazinyl or 5-methyl-imidazol-4-yl, then Q is other than

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Claims 11 to 22 (*cancelled*)